REMARKS

Claims 7-8 are pending herein and stand rejected under 35 U.S.C. § 103. In view of the arguments below, Applicants believe the claims are in condition for allowance. Reconsideration is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 7 and 8 under 35 U.S.C. 103(a) as being unpatentable over Gold *et al.* (U.S. 5,270,163) in view of Tullis (WO 88/09810) and Ferns *et al.* (Science 1991, vol. 253, pages 1129-1132). The Examiner proffers that Gold *et al.* teach a method for identifying nucleic acid ligands by a process of *in vitro* selection and amplification; that Tullis teaches nucleic acid conjugates comprising an antisense conjugated to a solubility modifying moiety that may be hydrophobic; and that Ferns *et al.* teach that inhibition of PDGF is a possible approach for prevention of restenosis following angioplasty. Office Action at 3.

The Examiner has deemed Applicants' arguments made in the prior response to this identical rejection unpersuasive. Specifically, the Examiner submits that, in contrast to Applicants' arguments, there is a reasonable expectation of success for the present invention. The Examiner states, "Because the art teaches that conjugation of nucleic acids to compounds that increase their solubility, cellular uptake and nuclease resistance was well-known in the art prior to the time of the invention and routine synthetic methods exist for producing such complexes, there is a reasonable expectation of success in combining the cited references regardless of whether some complexes may be non-functional and routine testing may be required to determine if the three dimensional structure of an aptamer has been affected by the conjugation." Office Action at 7-8.

Nucleic acid ligands are not equivalent to the nucleic acids described by Tullis. Nucleic acid ligands are an art-recognized class of molecule characterized by being nucleic acids that exhibit high specificity binding (typically in the nM or pM range) to a given target molecule. They are commonly referred to by the art-recognized term "aptamer". Although nucleic acid ligands are nucleic acids they represent an entirely different class of molecule to those nucleic acids that are important for the storage of information, or those that bind other nucleic acids purely upon complementary base pairing. Antisense nucleic acids do not rely on their three-dimensional shape to bind their complementary sequences. In the case of nucleic acid ligands, the three dimensional structure of the nucleic acid ligand is of key importance. An aptamer will

only bind target when it has assumed a complex three-dimensional structure, much like a denatured antibody cannot bind its target. Applicants submit that there was no reasonable expectation of success for obtaining a complex comprising a PDGF nucleic acid ligand and a Non-Immunogenic, High Molecular Weight Compound or Lipophilic Compound. Although Gold et al. teaches the SELEX method, Gold et al. does not provide a reasonable expectation that a functional PDGF nucleic acid ligand and a Non-Immunogenic, High Molecular Weight Compound or Lipophilic Compound will be obtained. The obvious problem of disruption of three dimensional structure of the nucleic acid ligand with the addition of a Non-Immunogenic, High Molecular Weight Compound or Lipophilic Compound mandates that this disclosure is much more than "routine testing required to determine if the three dimensional structure of an aptamer has been affected by the conjugation" (Office Action at 8), but rather a parameter that may have precluded any successful result. Thus, a reasonable expectation of success was not found in the prior art.

In determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); Schenck v. Nortron Corp., 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983) In Gillette Co. v. S.C. Johnson & Son, Inc., 919 F.2d 720, 725 (Fed. Cir. 1990) the Court stated, "we have consistently held that 'obvious to try' is not to be equated with obviousness." Additionally, in In re Tomlinson, 53 C.C.P.A. 1421, 363 F.2d 928, 931 (CCPA 1966) the court explained that "there is usually an element of 'obviousness to try' in any research endeavor, that . . . is not undertaken with complete blindness but rather with some semblance of a chance of success." Further, "An 'obvious-to try' situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued." In re Eli Lilly & Co., 902 F.2d 943, 945, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990). "'[O]bvious to try' is not the standard under § 103." In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). The recent KSR decision has not changed this standard. While a finite number of permutations may strengthen the obvious to try position –such is not the present case.

The combination of Gold et al., Tullis and Ferns et al., at most, yield an invitation to try. The disclosures of the cited references do not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued. There was nothing in the art to suggest that the functionality of the PDGF ligand would remain intact once complexed to the Non-Immunogenic, High Molecular Weight Compound or Lipophilic Compound. The Examiner has argued, "applicants appear to believe a prediction of therapeutic effect is required for a reasonable expectation of success in combining the cited references…. However, the examiner has made no representation regarding therapeutic efficacy of the claimed complex in combining the cited references because such efficacy is not required by the claims, which are directed to improvement of pharmacokinetic properties and targeting of therapeutic agents. The nucleic acid ligands of the instant invention are not therapeutic agents, claim 6 [sic] refers only to pharmacokinetic properties, not therapy…" This argument ignores the fact that pharmacokinetics is nothing more than the study of the behavior of drugs. The Examiner goes on to say that, "…claim 7 [sic] clearly recites the presence of a therapeutic agent in addition to the complex, not that the complex itself is a therapeutic agent. Therefore whether or not atamans have drawbacks as therapeutics is irrelevant to the rejection of record." Office Action at 7. Of course, claim 7 talks about the administration of the "Complex" to a patient. As such the complex by definition is a therapeutic.

Claim 7 requires, "A method for improving the pharmacokinetic properties of a PDGF Nucleic Acid Ligand comprising: covalently linking said PDGF Nucleic Acid Ligand with a Non-Immunogenic, High Molecular Weight Compound or Lipophilic Compound to form a Complex comprised of a PDGF Nucleic Acid Ligand and a Non-Immunogenic, High Molecular Weight Compound or Lipophilic Compound; and administering said Complex to a patient."

Claim 8 requires, "A method for targeting a therapeutic or diagnostic agent to a specific biological target that is expressing PDGF in a patient comprising: covalently linking said therapeutic or diagnostic agent with a Complex comprised of a PDGF Nucleic Acid Ligand and a Non-Immunogenic, High Molecular Weight Compound or Lipophilic Compound, and administering said Complex to a patient.

Both claims 7 and 8 comprise a complex comprised of a PDGF Nucleic Acid Ligand and a Non-Immunogenic, High Molecular Weight Compound or Lipophilic Compound. The definition of a PDGF Nucleic Acid Ligand can be found at page 20, lines 20-27 of the specification which reads, "'Nucleic Acid Ligand' as used herein is a non-naturally occurring Nucleic Acid having a desirable action on a Target. The Target of the present invention is PDGF, hence the term PDGF Nucleic Acid Ligand. A desirable action includes, but is not limited to, binding of the Target, catalytically changing the Target, reacting with the Target in a way which modifies/alters the Target or the functional activity of the Target, covalently attaching to the Target as in a suicide inhibitor, facilitating the reaction between the Target and another molecule. In the preferred embodiment, the action is specific binding affinity for PDGF, wherein the Nucleic Acid Ligand is not a Nucleic Acid having the known physiological function of being bound by PDGF." Thus the complex comprises a PDGF Nucleic Acid Ligand having the desirable action on a Target –a functional PDGF Nucleic Acid Ligand and a Non-Immunogenic, High Molecular Weight Compound or Lipophilic Compound. The disclosures of the cited references do not contain a sufficient teaching of how to obtain this desired result, or that this claimed result would be obtained if certain directions were pursued. Thus there is no reasonable expectation of success: there is not absolute predictability to be sure, but further there is no reasonable expectation of success. The art cited, at most, "piques the scientist's curiosity."

Finally, the Examiner states, "Applicants cite the Veronese publication as providing evidence that one of skill in the art would expect a loss of activity for a nucleic acid ligand upon PEGylation and that smaller molecules cannot be 'loaded' as heavily with PEG. Applicants conclude that the art does not provide an expectation of success with respect to using PEG to improve the pharmacokinetics of smaller (non-protein) drugs. This argument is not persuasive because, as noted previously, a 103 rejection does not require absolute predictability, merely a reasonable expectation of success." Applicants respectfully submit that the Veronese publication provides additional evidence that there was not reasonable expectation of success, let alone absolute predictability. The Veronese publication illustrates that it was not known in the art that the present disclosure could be successful. A reasonable expectation of success does not mean any hope of success. As stated above, "there is usually an element of 'obviousness to try' in any research endeavor, that . . . is not undertaken with complete blindness but rather with some semblance of a chance of success." Further, "An 'obvious-to try' situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a

result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued." In re Eli Lilly & Co., 902 F.2d 943, 945, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990). "'[O]bvious to try' is not the standard under § 103." In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). Applicants respectfully request reconsideration.

Closing Remarks

Applicants believe the claims are in condition for allowance give the arguments submitted above. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-5117 if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-5117.

Respectfully submitted,

Date: January 2, 2008

/Katherine Lobel-Rice/

Katherine Lobel-Rice, #58,079
Swanson & Bratschun, L.L.C.
8210 SouthPark Terrace
Littleton, Colorado 80120
Telephone: (303) 268-0066
Facsimile: (303) 268-0065

S:\ClientFolders\Gilead (formerly NeXstar)\Nex66\D2\NEX 66 D2 Response to OA dated 7-02-2007.doc